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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,166	08/31/2001	David R. Elmaleh	MGA-003.01	1584

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EXAMINER	
VIVLEMORE, TRACY ANN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/945,166	ELMALEH ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,11 and 25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,11 and 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection not reiterated in this Action is withdrawn.

Claim Rejections - 35 USC § 102

Applicant's amendments have overcome the rejections of record over Papahadjopoulos et al. and Rothschild et al. however, the following new rejections are made.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobori et al. (NeuroReport 1999 vol. 10, pages 2971-2974).

1. Claim 1 is directed to a targeted oligonucleotide construct comprising a targeting moiety, an oligonucleotide complementary to a nucleic acid of interest and an imaging agent suitable for use in PET, SPECT or MRI. Claim 4 states the oligonucleotide is an antisense oligonucleotide or oligonucleotide analog modified to enhance its efficacy, pharmacokinetic properties or physical properties. Claim 5 states the imaging agent is a radiolabel chosen from a list of radioisotopes. Claim 8 recites that the construct of claim 1 further comprises a therapeutic agent. Claim 11 limits claim 8 by reciting

limitations identical to those of claim 4. Claims 25-28 limit claim 1 and claims 30-33 and 34 limit claim 11 by reciting specific modifications to the antisense oligonucleotide portion of the construct.

2. Kobori et al. disclose phosphorothioate modified antisense oligonucleotides are conjugated with cholesterol at one end and an N-butyryl aminohexyl chain at the other end. This chain contains ^{11}C, a radioisotope listed in claim 5, at one position. Such oligonucleotides are able to enter cells and allow for real-time imaging of the construct inside cells and are used for a method of real-time imaging of mRNA expression. Thus, Kobori et al. disclose a construct containing a targeting moiety that is cholesterol, a small molecule, an oligonucleotide and ^{11}C, an imaging agent suitable for use in PET, SPECT or MRI. The antisense oligonucleotide of Kobori et al. is a therapeutic agent that is derivatized with phosphorothioate, which increases nuclease resistance and is specific for mRNA, meeting the limitations of claims 25-28, 30-32 and 34.

3. Thus, Kobori et al. disclose and anticipate claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34.

Claims 1, 4, 5, 8, 10, 11, 25, 26, 28, 30, 31 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Pardridge et al. (Proc. Natl. Acad. Sci USA 1995, vol. 92, pages 5592-5596).

4. Claim 1, 4, 5, 8, 11, 25, 26, 28, 30, 31 and 34 are described in the previous rejection. Claim 10 limits claim 8 by reciting several types of therapeutic agents, including radioisotopes.

5. Pardridge et al. disclose a PNA conjugated to biotin, a protein, and containing at one end a tyrosine labeled with ^{125}I, a radioisotope listed in claim 5. The instant specification states at page 7: " "Nucleic acid" refers to polynucleotides...[and] should also be understood to include, as equivalents, analogs of either RNA or DNA made from nucleotide analogs." PNAs are peptide nucleic acids, a nucleic acid analog made from nucleotide analogs. Thus, Pardridge et al. disclose a construct containing a targeting moiety that is biotin, a protein, an oligonucleotide and an imaging agent, ^{125}I, suitable for use in PET, SPECT or MRI. ^{125}I is a therapeutic agent that is a radioisotope, meeting the limitation of claim 10 and PNA is a nucleotide analog that is modified to increase nuclease resistance and is specific for mRNA, meeting the limitations of claims 25, 26, 28, 30, 31 and 34.

6. Thus, Pardridge et al. disclose and anticipate claims 1, 4, 5, 8, 10, 11, 25, 26, 28, 30, 31 and 34.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 11, 25-28, 30-32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobori et al. as applied to claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 above, and further in view of the following reasons.

7. Claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 are described in the 102 rejection over Kobori et al. Claim 2 limits claim 1 by stating the imaging agent is an unpaired spin atom, a free radical, a paramagnetic contrast agent or a metal chelate while claims 3, 6 and 7 recite specific examples of such imaging agents.

8. The teachings of Kobori et al. are described in the 102 rejection over this reference. Kobori et al. do not teach oligonucleotide constructs containing imaging agents that are unpaired spin atoms, free radicals, paramagnetic contrast agents or metal chelates.

9. It would have been obvious to one of ordinary skill in the art to modify the constructs disclosed by Kobori et al. that contain ^{11}C to be an unpaired spin atom, a free radical, a paramagnetic contrast agent or a metal chelate. One of ordinary skill in the art would recognize that unpaired spin atoms, free radicals, paramagnetic contrast agents, metal chelates and radioisotopes are all imaging agents used for PET, SPECT or MRI as evidenced by Applicant's own statements in the remarks submitted on June 13, 2005. Since one of ordinary skill in the art would recognize all of these compounds as imaging agents suitable for similar applications, the selection of one imaging agent over another is mere design choice that one of ordinary skill would make for various reasons including cost, stability or safety of a particular agent and suitability of a particular agent to a specific method of imaging.

10. Thus, the invention of claims 1-8, 11, 25-28, 30-32 and 34 would have been obvious, as a whole, at the time of invention.

Claims 1, 4, 5, 8, 11 and 25-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobori et al. as applied to claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 above, and further in view of Gewirtz et al. (US 5,098,890) and Low et al. (US 5,994,320).

11. Claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 are described in the 102 rejection over Kobori et al. Claims 29 and 33 limit claims 4 and 8, respectively, by reciting that the oligonucleotide portion of the construct is an antisense specific for the C-myb, N-myc, C-myc or PSA genes.

12. The teachings of Kobori et al. are described in the 102 rejection over this reference. Kobori et al. do not teach oligonucleotide constructs containing oligonucleotides that are antisense to C-myb, N-myc, C-myc or PSA genes.

13. Gewirtz et al. and Low et al. each teach antisense directed to C-myb. Low et al. teach at column 1, line 15 through column 2, line 25 that C-myb is involved in cellular proliferation and differentiation and that antisense to C-myb is known to inhibit proliferation of several cell lines.

14. It would have been obvious to one of ordinary skill in the art to modify the constructs taught by Kobori et al. wherein the oligonucleotide is an antisense targeting GFAP to one where the antisense targets C-myb. Kobori et al. and Low et al. provide a motivation to do so, Kobori et al. teaching that oligonucleotide constructs allow for real-time imaging of mRNA expression in a cell and Low et al. teaching that targeting of C-myb is desirable because of its role in cellular proliferation. One of ordinary skill in the art would have had a reasonable expectation of success in making the construct of Kobori et al. with an antisense targeted to C-myb because Kobori et al. actually make

their construct using techniques well-known in the art and Low et al. and Gewirtz et al. actually make antisense to C-myb using similar synthetic techniques.

15. Thus, the invention of claims 1, 4, 5, 8, 11 and 25-34 would have been obvious, as a whole, at the time of invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811.

On July 15, 2005, the Central FAX Number was changed to 571-273-8300. Faxes sent to the old number (703-872-9306) will be routed to the new number until September 15, 2005.

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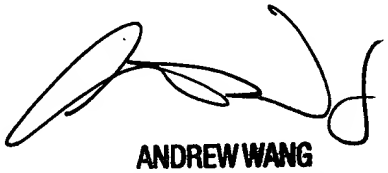

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Tracy Vivlemore
Examiner
Art Unit 1635

TV
August 17, 2005